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10/777,211	02/13/2004	Markku Anttila	2630-127	2487

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EXAMINER

GEMBEH, SHIRLEY V

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/777,211	Applicant(s) ANTTILA, MARKKU	
	Examiner Shirley V. Gembeh	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6/28/05; 6/8/04</u> | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 28th, 2005 and June 8th 2004 has been received and acknowledged.

Status of claims:

Claims 1-9 are pending.

Claims 1-9 are rejected.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 6 and 8-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With regards to claim 1 it is also not apparent what step in the recited process would or would not have been the enhancing step. It is not apparent from the claim that administration with food would have an effect of enhancing bioavailability, or whether it is the oral administration

As to claim 2 it is not clear how this compound ospemifene further limits claim 1 when the formulation for same is already recited in claim 1.

Claim 6 recites capable of, what does capable of mean? With regards to foodstuff how does this define food stuff

Claim 9 recites the limitation "the symptoms ". There is insufficient antecedent basis for this limitation in the claim 8. Thus, claim 8 and its dependent claim 1 are properly included in this rejection. Also, how is urinary or vaginal symptom related to osteoporosis and why would symptoms of osteoporosis be urinary or vaginal?

Claim Rejections - 35 USC § 112

Claims 7 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating osteoporosis, does not reasonably provide enablement for preventing osteoporosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988)):

- 1) Nature of invention.
- 2) State of prior art.
- 3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure
- 4) Level of predictability in the art.
- 5) Amount of direction and guidance provided by the inventor.
- 6) Existence of working examples.
- 7) Breadth of claims.

8) Level of ordinary skill in the art.

See below:

In the instant case, applicants are claiming in part, a method of preventing a osteoporosis in a mammal (claim 1), through enhancing the bioavailability of a therapeutically active compound administering orally the compound with food.

1) Nature of the invention.

The nature of the invention is directed to methods of treating/preventing in a mammal to alleviate the pathological effects of osteoporosis. As stated, however, claim 1 includes within its scope all types of osteoporosis such as postmenopausal osteoporosis (primary), senile osteoporosis (Primary), secondary osteoporosis, idiopathic juvenile osteoporosis (Primary)

A. Treatment by osteoporosis

There are several types of osteoporosis naming a few such as postmenopausal osteoporosis (primary), senile osteoporosis (Primary), secondary osteoporosis, idiopathic juvenile osteoporosis (Primary)

Up to date there is no one particular antbone loss agent that is effective for all forms of bone disorder. (see www.surgeongeneral.gov/library/bonehealth/chapter_9.html) page 2
key message. There is no one treatment, or combination of treatments which provides prevention (not occurring even the first time) of a bone disorder of anytime. The best prevention, however, is a life-long commitment to physical activity, good nutrition, and

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normal reproductive hormone status. (See

www.endocrineweb.com/osteoporosis/treatment.htmlWeb), however, this is not

prevention, all of which help reduce osteoporosis (for example one type of bone disease) but do not prevent.

As discussed below, (see

<http://www.endocrineweb.com/osteoporosis/treatment.html>), teaches that researchers face the problem of sifting through potential conditional drugs for osteoporosis to find ones promising enough to make. Treatment of osteoporosis is classified in two groups and non of the drugs have proven themselves yet (see www.endocrineweb.com/osteoporosis/treatment.html). While the state of the art is relatively high with regard to the treatment of osteoporosis with specific agents, for a compound or genus to be effective against bone disease generally is contrary to medical science. Thus a considerable amount of invivo and invitro testing is required before the agent can be considered for a particular type of disease.

B. Chemotherapy

www.endocrineweb.com/osteoporosis/treatment.html teaches that There is no one treatment, or combination of treatments which provides prevention (not occurring even the first time) of fractures due to osteoporosis. At the present time, only anti-resorbers are approved in the United States by the FDA for use in treating osteoporosis and none of the drugs in this group have demonstrated prevention.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Further, their mode of action is often unknown or very unpredictable and administration of the drugs can be accompanied by undesirable side effects.

2) State of the prior art and the predictability or lack thereof in the art.

The state of the prior art is that it involves a myriad of diseases such as osteoporosis such as postmenopausal osteoporosis (primary), senile osteoporosis (Primary), secondary osteoporosis, idiopathic juvenile osteoporosis (Primary) thus preventing or treating will include screening *in vitro* and *in vivo* to determine the effect of the compound on the specific disease. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant claimed invention is highly unpredictable as discussed below:

Thus, in the absence of a showing of correlation between all the conditions associated with bone disease claimed as capable of being treated by the compounds of the instant claims, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compounds due to the unpredictability of the role of bone fracture for example.

3) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The quantity of experimentation needed is undue experimentation. One of ordinary skill in the art would first need to determine the type of conditions associated with bone loss and then determine which of the thousands of compounds would be suitable for said treatment and/or prevention. Note that osteoporosis is only one such condition. There are others, e.g., osteoporosis such as postmenopausal osteoporosis (primary), senile osteoporosis (Primary), secondary osteoporosis, idiopathic juvenile osteoporosis (Primary) etc for which the current specification provides no guidance.

4) Level of predictability in the art.

The art pertaining to the treatment of all bone disease remain highly unpredictable. As disclosed above, there is no absolute predictability even in view of the seemingly high level of skill in the art. Firstly, for a compound or genus to be effective against osteoporosis for example or a bone disease generally is contrary to medical science. Conditions associated with bone disease is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the conditions associated with bone loss reaction. Accordingly, treatments for conditions associated with bone loss/bone mass density are normally tailored to the particular type of mediator present, as there is no, and there can be no "magic bullet" against all conditions associated with bone loss related diseases generally.

5) Amount of direction and guidance provided by the inventor.

The amount of direction or guidance present is not sufficient to claim such a broad array of bone disorder. However, the gap between the teaching in the specification of *in vitro* activity and *in vivo* is large enough to warrant thorough and compelling *in vivo* data especially in the absence of working examples demonstrating the full scope of all bone diseases.

6) Existence of working examples.

As discussed above, the working example found on pages 6-8 in no way correlates to preventing all types of bone disease. Applicant's omission of working examples does not enable one of ordinary skill in the art to treat the numerous amounts of diseases encompassed by the instant invention.

7) Breadth of claims.

Claim 1 is extremely broad due to the vast number of possible diseases encompassed by the instant invention.

8) Level of ordinary skill in the art.

Due to the unpredictability in the pharmaceutical art (see reference www.endocrineweb.com/osteoporosis/treatment.html Web), it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Hence, the specification fails to provide sufficient support of the broad use of the compounds of the claims for the treatment of any disease. As a result necessitating one of ordinary skill in the art to perform an exhaustive search to determine which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

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Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Atrophic change in the skin has been noted as a prominent part of the aging process. The only way possible is to stop aging and that is not possible, therefore how is skin atrophy prevented?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biskobing Expert Opinion Invest. Drug taken with of WO 97/32574 in view of Halonen et al. US 6,245,819).

Biskobing teaches the current claims 1 and 2 administering the drug ospemifene (see abstract) to treat bone loss as in claim 7.

WO teaches the same compound, structurally identical to that of the claimed subject matter. The reference also teaches the compound can be taken with other

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active compounds. Thus food is can be active agent as it comprises nutrients for the functioning of the body. Thereby teaches the instant claim 6.

Halonen et al (US'819 hereafter) teaches FC127a(=deaminohydroxytoremifene) as well as active metabolites, geometric isomers or stereoisomers thereof, (see col. 2 lines 35-59). US'819 teaches the said compound and the its medical use in the treatment of vaginal dryness and sexual dysfunction, see abstract. As self evidenced by the instant claims (see claims 8 and 9), the treatment of symptoms related to skin and mucosal atrophy such as vaginal dryness, dyspareunia via inhibition of skin or mucosal atrophy is inherently met and it is naturally occurring when the therapeutically effective amount of FC1271a is administered. Bioavailability can be affected by factors such as the rate at which a tablet or capsule dissolves, binding products using in formulating the medication, and the person's ability to break down and use the medication.

It is noted that ospemifene is FC127a (=deaminohydroxWoremifene) that has the chemical structure recited in instant claim 1. Thus, all the critical elements required by the instant claims are well taught and the scope of the claimed subject matter is well embraced and not patentably distinct over the prior ad of the record.

Although, the reference, did not per se teach bioavailability of the compound, bioavailability is defined as a term used in describing the amount of a medication taken that is actively available to the targeted body area. Bioavailability can be affected by factors such as the rate at which a tablet or capsule dissolves, binding products using in formulating the medication, and the person's ability to break down and use the

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medication. Thus obvious since the compound is the same having the same structure will necessarily have the characteristics of bioavailability.

Also, the combined references did not teach how to administer the drug specifically when to take the drug in claims 3-5, however, from the teachings of WO/9732574 indicates (see page 3 lines 1-10) suggesting that there are other methods of administration. This also is within the purview of the skilled artisan to determine when and how to administer the composition. It is well known to the skilled artisan that most drugs are administered based on the effect on the individual, while some patients can administer the drug on an empty stomach with water, other population may need to have food prior to administering or after administering. The skilled artisan would have been motivated to combine the above cited references and expect a degree of success in the treatment of bone loss, vaginal and urinary symptoms as all critical elements required by the instant claims are well taught and the scope of the claimed subject matter is well embraced and not patentably distinct over the prior art of the record.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

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by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

I. Claims 1-9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent Application No. 10783092. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

Both sets of claims refer to using the same compound ospemifene enhancing bioavailability to treat various types of diseases-osteoporosis (claim 7) in the current application (claims 1 -9) and osteoporosis (claims 1 – 11) in the copending

application. The current application claims anticipate the copending application claims

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

II. Claims 1-9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent Application No. 11183185. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

Both sets of claims refer to using structurally similar core compound ospemifene a SERM compound in the current application (claims 1 -9) and a SERM receptor modulator having the same chemical structure (claims 1 – 13) in the copending application. The current application claims anticipate the copending application claims

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

III. Claims 1-9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent Application No. 11201098. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

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Both sets of claims refer to using structurally similar core compound ospemifene a SERM compound in the current application treating skin atrophy (claims 1 -9) and a SERM compound ospimifene treating skin atrophy (claims 1-12) in the copending application. The current application claims anticipate the copending application claims

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

IV. Claims 1-9 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6984665. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

Both the claims of the application and the patented claims refer to using the same compound ospemifene enhancing bioavailability to treat various types of diseases-vaginal symptoms in the current application (claims 1 -9) and urogenital atrophy (claims 1 -3) in the patent application. The current application claims anticipate the copending application claims

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

No claim is allowed.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembah whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SVG
4/18/06


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